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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/026,882	02/19/98	ROSENBLUM M	D5442C/CIP

HM12/1227

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EXAMINER	
HUFF, S	
ART UNIT	**PAPER NUMBER**
1642	7

DATE MAILED: 12/27/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/026,882	Applicant(s) Rosenblum
	Examiner Sheela J. Huff	Group Art Unit 1642

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-17* is/are pending in the application.

Of the above, claim(s) *1-7, 16, and 17* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *8-15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This application is a CIP of 08702205, which is a CON of 08/312558, which is a CON of 07/866693.

Election/Restriction

2. Applicant's election without traverse of Group I, claims 8-15 in Paper No. 6 is acknowledged.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

Claim Rejections - 35 USC § 112

4. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating neoplastic cells with the disclosed conjugate, does not reasonably provide enablement for prevention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant claims that the conjugate composed of a protein that binds CD33 and gelonin can prevent the recurrence of a neoplastic condition. While the specification does show that the mice treated with the conjugate have a slower tumor growth rate and that no tumor are seen for up to 5 months, this does no enable prevention. "Prevention" implies that the neoplastic condition never occurs and this is not what applicant has demonstrated. In fact, complete prevention is hard to achieve. In view of the lack of examples to show a complete prevention and in view of the state of the art which recognizes that "preventions" are rare, it is the Examiner's position that undue experimentation would be required by one skilled in the art to make and use the instant invention.

5. Claims 8-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is dependent on non-elected claim 6.

6. Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 12 is directed to prevention and "prevention" does not further limit "treating".

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanimoto et al, Leukemia, vol. 3 p. 339 (1989) or Scheinberg et al, Leukemia, vol. 3 p. 440 (1989) in view of Thorpe et al, Immunological Reviews vol. 62 p. 119 (1982) and Andrews et al Blood, vol. 62 p. 124 (1983) and Rosenblum et al US 5631348 (filed 8/14/90).

Tanimoto et al and Scheinberg et al each teach monoclonal antibody M195, an antibody which specifically binds to CD33. The references further teach the potential of using M195 as a therapeutic agent as a carrier of toxins or alpha emitting isotopes for the treatment of ANLL (page 444 of Scheinberg et al or page 347 of Tanimoto et al).

The only difference between the instant invention and the reference is that the primary references do not specifically show the therapeutic aspect nor do the references teach the formation of a conjugate of M195 with gelonin nor do the references teach the use of recombinant gelonin or active fragments of gelonin.

Thorpe et al teach conjugation of antibodies to toxic moieties including gelonin for effective cell killing which would have potential in therapeutic applications (see pages 147-150). In fact, they specifically state, on page 147, that even though 90% of the gelonin conjugates were inactivated by the act of conjugation they still retained a remarkably high rate of cell killing.

Andrews et al teach that monoclonal antibodies reactive with CD33 may be useful for the treatment of leukemia for in vivo or in vitro use (the in vitro use being the deletion of malignant bone marrow in autologous bone marrow transplantation).

Rosenblum et al shows that gelonin can be may recombinantly and active fragments can be isolated.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the antibody conjugates as taught by the primary references to treat neoplastic cells in vitro or in vivo. The motivation comes from the primary references which clearly suggest the use of conjugates of M195 and toxin to treat leukemia (page 444 of Scheinberg et al or page 347 of Tanimoto et al). The use of gelonin as the toxin would have been obvious in view of Thorpe et al, who shows that gelonin is very effective for killing cells. The use of recombinant gelonin or active fragments is within the purview of one skilled in the art (especially in view of Rosenblum et al).

10. Claims 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scheinberg US 5730982 (filed 12/14/89) in view of Thorpe et al, Immunological Reviews vol. 62 p. 119 (1982) and Andrews et al Blood, vol. 62 p. 124 (1983) and Rosenblum et al US 5631348 (filed 8/14/90).

Scheinberg teaches monoclonal antibody M195, an antibody which specifically binds to CD33. The reference further teaches the use of M195 in a conjugate with a

cytotoxic agent, wherein the cytotoxic agent can be a toxin (col. 6, lines 9-13). The reference further disclose the use of conjugate to treat acute or chronic leukemia *col. 6, lines 17-29). **Applicant is also directed to the claims of this patent.**

The only difference between the instant invention and the reference is that the primary reference does not specifically show the therapeutic aspect, teach the formation of a conjugate of M195 with gelonin nor does the reference teach the use of recombinant gelonin or active fragments of gelonin.

Thorpe et al teach conjugation of antibodies to toxic moieties including gelonin for effective cell killing which would have potential in therapeutic applications (see pages 147-150). in fact, the specifically state, on page 147, that even though 90% of the gelonin conjugates were inactivated by the act of conjugation they still retained a remarkably high rate of cell killing.

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It would have been obvious to one of ordainry skill in the art at the time of the invention to use the antibody conjugates as taught by the primary references to treat neoplastic cells in vitro or in vivo. The motivation comes from the primary references

which clearly suggest the use of conjugates of M195 and toxin to treat leukemia (see col 6 of US 5730982). The use of gelonin as the toxin would have been obvious in view of Thorpe et al, who show that gelonin is very effective for killing cells. The use of recombinant gelonin or active fragments is within the purview of one skilled in the art (especially in view of Rosenblum et al).

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is (703) 305-7866. The Examiner can normally be reached on Monday, Wednesday and Thursday from 6:30am to 4:00pm.

If attempts to teach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached on (703)308-4310.

The FAX phone number for the group is (703)308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**paula.hutzell@uspto.gov**].

All Internet e-mail communications will be made of record in the application file.

PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

Sheela J. Huff
December 15, 1999

Sheela J. Huff
Primary Examiner